Proposal for Streamlining the SDRG and ADRG Authoring Process

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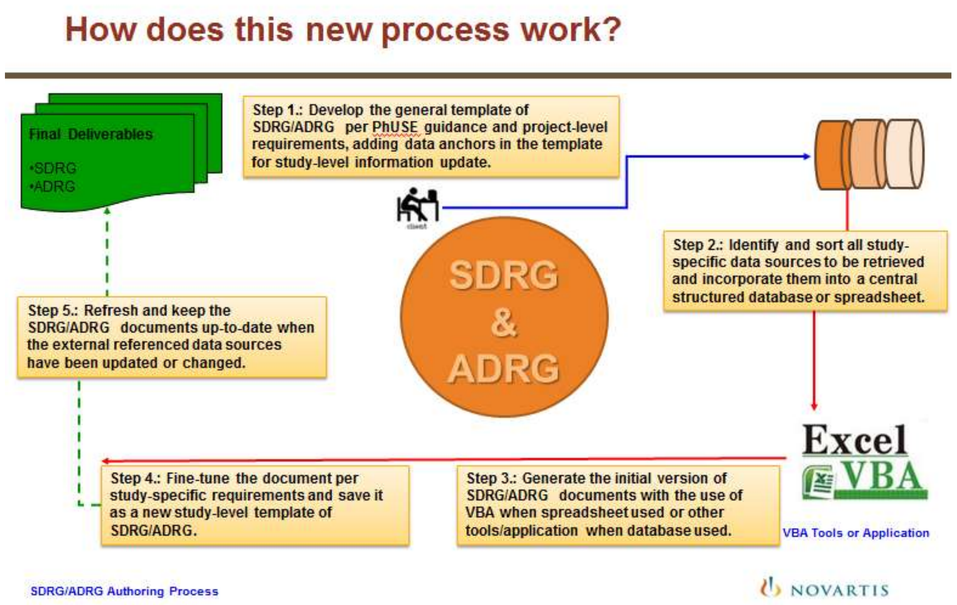
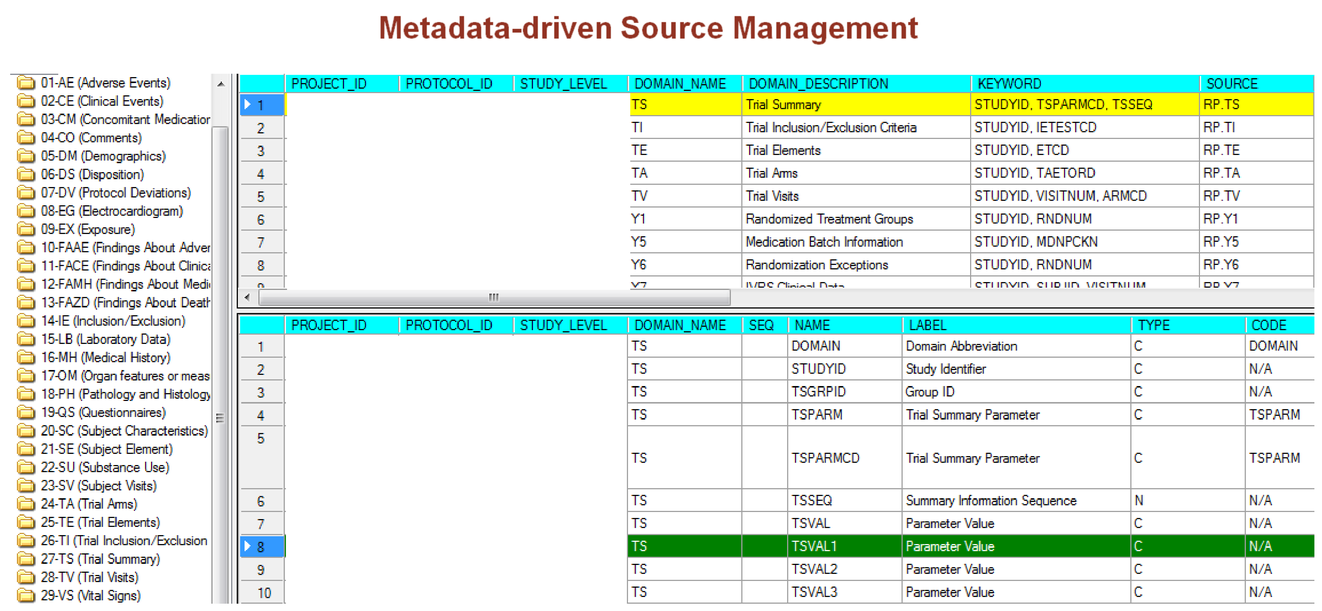
Introduction

SDRG and ADRG are now part of e-submission package, providing FDA reviewers a single point of orientation of submission datasets. These documents incorporate additional information as well as some duplication from other submission documents. The authoring process of these two key documents could be time-consuming and tedious, considering most of the included information may exist in different datasets, documents. Keeping up with changes on an ongoing basis and inconsistency may be a potential problem as well.

Data Flow and Working Process





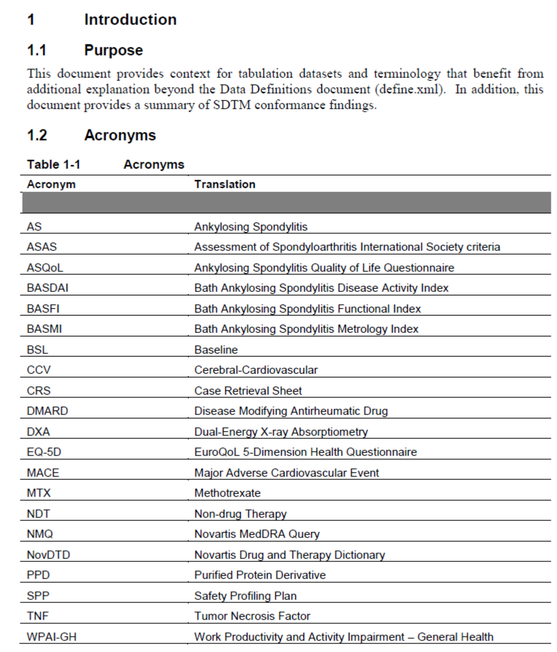
Method

To simplify the authoring process, a centralized metadata-driven method is proposed to streamline and automate this activity. All data sources, including but not limit to study-level metadata repository, SDTM/ADaM datasets, central comments log, OpenCDISC validation reports, etc. will be identified in advance and retrieved them into a central structured database or spreadsheet. A corresponding VBA tool or user-friendly interface application will be developed to facilitate this authoring process by incorporating all of the related information and generating the SDRG/ADRG documents automatically, making sure all contexts be consistent across different sources accordingly.

Results

The use of new process will result in:

- Substantially improved quality of SDRG/ADRG authoring due to the standardization of methods across the team members as well as projects/studies.
- Greater productivity and efficiency by being able to deliver common SDRG/ADRG documents in a few hours, compared to a few days with the traditional way.
- Highly consistency and real-time synchronization of major contents when multiple sources of the SDRG/ADRG have been updated or changed accordingly.



1 Introduction

1.1 Purpose

This document provides context for tabulation datasets and terminology that benefit from additional explanation beyond the Data Definitions document (define.xml). In addition, this document provides a summary of SDTM conformance findings.

1.2 Acronyms

Table 1-1 Acronyms

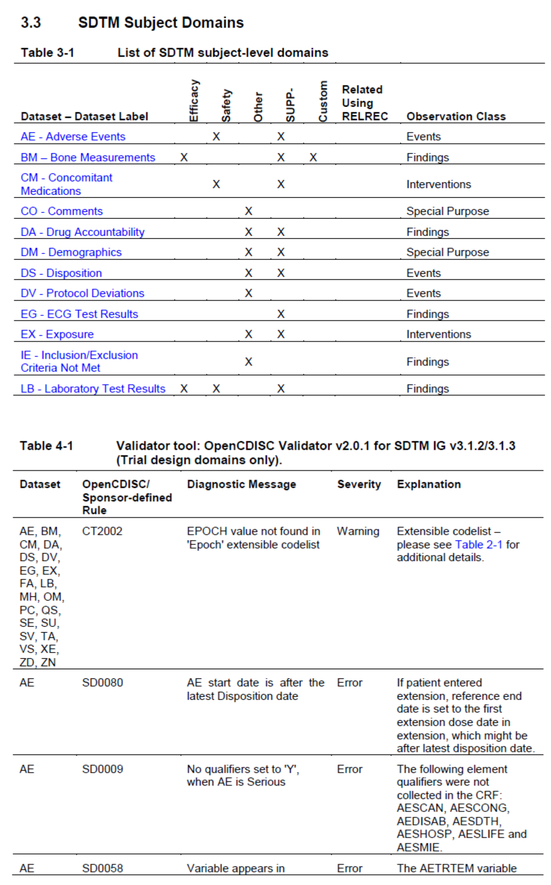
Acronym	Translation
AS	Ankylosing Spondylitis
ASAS	Assessment of Spondyloarthritis International Society criteria
ASQoL	Ankylosing Spondylitis Quality of Life Questionnaire
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BASMI	Bath Ankylosing Spondylitis Metrology Index
BSL	Baseline
CCV	Cerebral-Cardiovascular
CRS	Case Retrieval Sheet
DMARD	Disease Modifying Antirheumatic Drug
DXA	Dual-Energy X-ray Absorptiometry
EQ-5D	EuroQoL 5-Dimension Health Questionnaire
MACE	Major Adverse Cardiovascular Event
MTX	Methotrexate
NDT	Non-drug Therapy
NMQ	Novartis MedDRA Query
NovDTD	Novartis Drug and Therapy Dictionary
PPD	Purified Protein Derivative
SPP	Safety Profiling Plan
TNF	Tumor Necrosis Factor
WPAI-GH	Work Productivity and Activity Impairment – General Health

2.3.4 TI – Trial Inclusion/Exclusion Criteria

The trial inclusion/exclusion criteria were not fully described in the TI domain due to the 200 character limit of IETEST. Please refer to Appendix I for the full text of the criteria.

2.3.5 TS – Trial Summary

In order to be able to use the functionality of explaining the null values that may appear for TSVAL in the Trial Summary domain, Version 3.1.3 of SDTM was applied. In addition, to allow for more than 200 characters in TSVAL when the value for TSPARM was free text, an additional column (e.g., TSVAL1) was added as recommended on page 249 of the SDTM implementation guide Version 3.1.2.



3.3 SDTM Subject Domains

Table 3-1 List of SDTM subject-level domains

Dataset – Dataset Label	Efficacy	Safety	Other	SUPP-	Custom	Related Using RELREC	Observation Class
AE - Adverse Events		X		X			Events
BM – Bone Measurements	X			X	X		Findings
CM - Concomitant Medications		X		X			Interventions
CO - Comments			X				Special Purpose
DA - Drug Accountability			X	X			Findings
DM - Demographics			X	X			Special Purpose
DS - Disposition			X	X			Events
DV - Protocol Deviations			X				Events
EG - ECG Test Results				X			Findings
EX - Exposure			X	X			Interventions
IE - Inclusion/Exclusion Criteria Not Met			X				Findings
LB - Laboratory Test Results	X	X		X			Findings

Table 4-1 Validator tool: OpenCDISC Validator v2.0.1 for SDTM IG v3.1.2/3.1.3 (Trial design domains only).

Dataset	OpenCDISC/ Sponsor-defined Rule	Diagnostic Message	Severity	Explanation
AE, BM, CM, DA, DS, DV, EG, EX, FA, LB, MH, OM, PC, QS, SE, SU, SV, TA, VS, XE, ZD, ZN	CT2002	EPOCH value not found in 'Epoch' extensible codelist	Warning	Extensible codelist – please see Table 2-1 for additional details.
AE	SD0080	AE start date is after the latest Disposition date	Error	If patient entered extension, reference end date is set to the first extension dose date in extension, which might be after latest disposition date.
AE	SD0009	No qualifiers set to 'Y', when AE is Serious	Error	The following element qualifiers were not collected in the CRF: AESCAN, AESCONG, AEDISAB, AESDTH, AESHOSP, AESLIFE and AESMIE.
AE	SD0058	Variable appears in	Error	The AETRTEM variable

Conclusion

This process proposal, together with the development of an user-friendly interface, could significantly facilitate the SDRG/ADRG authoring process with higher efficiency and quality. Moreover, this proposal could minimize the inconsistency between the SDRG/ADRG documents when multiple sources were used.